

Non-technical Abstract

This study evaluates the benefit of being injected with a preparation of genetically modified fibroblasts (skin cells) made from the patients' own skin. This trial will be available for patients whose tumor has spread beyond the limits that are curable by surgery or other standard treatments. While it is not possible to predict whether the patients will receive any personal benefit from the participation in this study, information may be derived that may be helpful to others with a similar disease.

Before beginning treatment, physician will perform a history and physical examination. The patient will have blood tests (approximately 6 tablespoons of blood will be drawn), a urinalysis, a chest x-ray, an electrocardiogram, and CT or MRI scans performed. Blood will be drawn on days 0 (pre-treatment), 7, 14, 21, 28, 35, and 42.

In order to perform this study, fibroblasts will be prepared. These are cells that normally reside in the skin. In order to obtain these cells, a piece of the patient's skin ($\frac{1}{2}$ inch wide and 2 inches long) will be removed at the time of obtaining the tissue samples for confirmation of the diagnosis of my tumor or at the separate time. When enough of these cells have been obtained, the fibroblasts will be transformed with cancer-fighting human genes (called interleukin-12, IL-12) using a vehicle made from mouse virus and capable of inserting genes into these cells. This engineered virus, which is used strictly as a "transportation system," will also contain a bacterial gene which serves as a marker so the investigators can locate the cancer-fighting genes. This new gene will enable the fibroblast skin cells to make a normal human protein called IL-12, which is usually made in very small amounts only by cells of the immune system. Interleukin-12 is thought to stimulate an immune response to the tumor cells in the preparation. This immune response may

make tumors shrink as they have done in a previous trial of IL-12 gene therapy conducted at the University of Pittsburgh.

Approximately 3 - 4 weeks after the skin biopsy has been obtained, the fibroblasts that are making interleukin-12 will be injected into one or two of the tumors that are easily accessible, such as those lying in the skin or mucosa using a very small needle. These sites will be marked with permanent india ink so that their location will be known. Each site will contain fibroblasts making interleukin-12 or not making any interleukin-12 at all. The patient is required to return to the clinic the day following these injections for the purpose of evaluating any side effects. A total of four injections will be carried out. Twenty eight days after the first injections, two injection sites will be biopsied under local anesthesia. These biopsies will require a few skin stitches each. The pieces of skin that are removed will be examined for evidence that the approach is having the expected immunologic effects. Lastly, the patients are required to return to the clinic one and two months after the last injections to evaluate progress.